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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/758,036	LEBERER ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,20,21 and 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,20,21 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 29, 2003 has been entered.

Claims 1-10, 20, 21 and 25 are pending and under consideration in the instant application. Any rejection of record in the previous Office Action, mailed January 29, 2003, that is not addressed in this action has been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **This is a new rejection that is necessitated by amendment.**

Claim 2 recites the limitation "TOM" in the second line of the claim. There is insufficient antecedent basis for this limitation in the claim. The previous claim, indeed the entire specification, lacks any reference to the term "TOM" making it impossible to determine the metes and bounds of the limitation.

Miscellaneous Comments

Applicant's traversal of the finality of the previous Office Action was addressed in the Advisory Action mailed January 28, 2004. Briefly, Applicant was pointed to the sections of the MPEP discussing the treatment of claims objected to as being improperly multiply dependent. As Applicant has provided no further argument regarding this matter, and the Finality of the Office Action has been removed as a result of the filing of a request for continued examination, the point is now considered moot.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3, 20 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaber in view or Ketchum and Fairman, as set forth in the previous Office Actions. **This rejection is maintained for the reasons set forth in the previous Office Actions.**

Claims 1-10, 20, 21 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaber in view or Ketchum and Fairman as applied to claims 1-3, 20 and 21 above, and further in view of Tang and Rampe, as set forth in the previous Office Actions. **This rejection is**

maintained for the reasons set forth in the previous Office Actions, and is now applied to newly added claim 25.

With regard to the added limitation set forth in claim 25, it would be obvious to use IRK1 in the assay because Tang teaches that IRK1 and gpIRK1 are functionally equivalent, having 99% amino acid identity, as well as conserved structures (such as a pore region and two transmembrane domains) that are associated with the functional ability to transport potassium ions into the cell (see for example the Abstract and page 1233, right column first and second full paragraphs). This fact, coupled with the expressed ability to use any potassium ion channel in the assay (see for example Gaber, column 3, lines 10-13), provides the requisite level of obviousness, motivation and expectation of success to make claim 25 also obvious when considering the teachings of Gaber in view or Ketchum and Fairman and further in view of Tang and Rampe.

Response to Arguments Concerning Claim Rejections - 35 USC § 103

Applicant's arguments filed December 29, 2003 have been fully considered but they are not persuasive. Applicant provides the following grounds of traversal, which apply equally to both rejections as set forth above (i.e., Gaber in view or Ketchum and Fairman, and Gaber in view or Ketchum and Fairman in view of Tang and Rampe):

1. Applicant argues that one of skill in the art would have been led away from the teachings of Fairman because one of ordinary skill in the art would have expected that the deletion of *TOK1* from a strain already deleted in *TRK1* and *TRK2* (i.e., the *trk1Δ trk2Δ* double mutant strain) would exhibit a more extreme pathology (i.e., have a worse phenotype as it regards potassium

metabolism). Indeed, Applicant recognizes that Fairman confirms that the *tok1Δ trk1Δ trk2Δ* triple mutant grows more poorly than the *trk1Δ trk2Δ* strain.

2. Applicant argues that the disclosure of their specification indicates that human potassium ion channels HERG1 and Kv1.5 were unable to complement the *trk1Δ trk2Δ* strain, and therefore one of skill in the art would presume that they would be equally unable to complement the *tok1Δ trk1Δ trk2Δ* triple mutant owing to its more pathogenic phenotype. Applicant argues that this finding abolishes any motivation to test any eukaryotic potassium ion channel in the *tok1Δ trk1Δ trk2Δ* triple mutant, because it represents an unexpected result.

3. Applicant argues that they discovered that the triple mutant, in contrast to the findings of Fairman, was not more pathogenic than the *trk1Δ trk2Δ* strain, thus Applicant's invention represents an unexpected result.

Applicant's arguments are not convincing for the following reasons:

1. Applicant acknowledges that the phenotype of an *S. cerevisiae* strain deleted for *TRK1 TRK2* and *TOK1* has a more pathological phenotype than a strain deleted for *TRK1* and *TRK2* alone, this being measured by the ability of the strain to grow under potassium ion limiting conditions. An artisan possessing ordinary skill in the art of yeast genetics would immediately recognize the epistatic relationship between the *TRK1*, *TRK2* and *TOK1* genes as demonstrated by Fairman, coming to the obvious conclusion that the *TOK1* gene can at least partially compensate for the loss of *TRK1* and *TRK2*. Coupled with the biochemical knowledge that *TOK1* indeed has the biochemical capacity to transport *TOK1* into the cell (as taught by Ketchum), the ordinary skilled artisan would recognize that the presence of *TOK1* in a cell deleted for both *TRK1* and *TRK2* would affect the sensitivity of an assay that measures the ability of a heterologous potassium ion

channel to compensate for the loss of potassium ion transport in a cell (such as the assay taught by Gaber). In other words, the presence of the third potassium ion transporter (*TOK1*) will interfere with the testing of a heterologous protein for its ability to complement the loss of potassium ion transport in a yeast cell that has not been completely deleted for potassium ion transport activity (i.e., only *TRK1* and *TRK2* are deleted). Thus, Applicant's allegation that the more pathological phenotype of the triple mutant strain would lead one of skill in the art away from the teachings of Fairman as it applies to the assay described by Gaber is in fact the *motivation* for one of skill in the art to gravitate towards the teachings of Fairman. Indeed, one of skill in the art who was practicing the assay of Gaber would observe the teachings of Fairman, and logically come to the conclusion that the most accurate manner in which to perform the assay would be to inactivate *all three* of the potassium ion transporters in yeast, as taught by Fairman. Thus, this argument made by Applicant simply strengthens the motivation to combine the teachings of Gaber and Fairman.

2 and 3. Applicant's argument that, based upon the teachings set forth in the instant specification (i.e., that neither HERG1 or Kv1.5 could rescue the *trk1Δ trk2Δ* strain and that the double deletion is phenotypically worse than the triple deletion), one would be dissuaded from performing the assay of Garber in the triple deletion strain taught by Fairman, is misplaced for several reasons which are discussed below.

First, the knowledge that neither HERG1 nor Kv1.5 were able to complement the *trk1Δ trk2Δ* strain was not common knowledge to the skilled artisan prior to the instant invention; as such, this information could not have prevented the ordinary skilled artisan from being motivated to combine the teachings of Garber in view of Ketchum and Fairman because it was unknown to

that same ordinary skilled artisan when the combination would have been made. Indeed, the art indicates the opposite of what Applicant argues, where the triple deletion is phenotypically worse than the double deletion (Fairman) and where a eukaryotic potassium channel has the ability to complement the double deletion strain (Tang). The simple fact of the matter is that the skilled artisan had obvious reasons to combine the teachings of Gaber in view of Fairman and Ketchum as well as a scientifically sound motivation and a reasonable expectation of success at the time the teachings were available in the prior art. It is important to note that the rejection was not predicated on hindsight reasoning (i.e., the Office did not reconstruct the rejection by piecing together Applicant's invention based on their own disclosure), thus the Office cannot consider the inability of either HERG1 or Kv1.5 to complement the *trk1Δ trk2Δ* strain when establishing a rejection, provided that there was sufficient obviousness, motivation and expectation of success at the time the teachings were available as prior art. This is especially true in light of the fact that there are indeed eukaryotic potassium ion transporters that can complement the *trk1Δ trk2Δ* strain, as is obvious from the fact that gpIRK1 *in the very least* does so, as taught by Tang (see for example the Abstract), and that the triple deletion has a more compromised phenotype than the double deletion (as taught by Fairman). Therefore, the ordinary skilled artisan would at least be motivated to combine the teachings of the indicated references to arrive at the invention insofar as it related to the gpIRK1 potassium ion channel even in view of Applicant's arguments concerning the non-complementation of HERG1 and Kv1.5.

Second, the presumption that a protein (such as HERG1 or Kv1.5) would be unable to rescue a triple deletion strain, simply because it was unable to rescue a double deletion strain, is not scientifically sound. The ordinary skilled artisan can easily envision a situation where the

Tok1 protein would interfere with the activity of HERG1 or Kv1.5 by competing for one or more co-factors required for activity, thereby negating the activity of either or both proteins and resulting in the absence of complementation. When envisioning this plausible situation, the skilled artisan would be even more motivated to use the triple deletion strain in order to ensure that the Tok1 protein was not acting in an interfering capacity with regard to the HERG1 and/or Kv1.5 proteins. Indeed, the argument presented by Applicant seems to contradict their own findings that HERG1 and Kv1.5 were unable to rescue the double mutant strain while being able to rescue the triple mutant strain. Significantly, regarding Applicant's assertion that the double deletion strain is worse than the triple deletion strain, this result directly contradicts the teachings of the prior art (Fairman), for which Applicant provides no explanation.

Finally, even if one of ordinary skill in the art were to accept Applicant's allegation that non-complementation of a double deletion strain by HERG1 nor Kv1.5 would abrogate any motivation to test these proteins in a triple deletion strain, Applicant's argument amounts to an "unexpected results" argument which requires that the claims in question be commensurate in scope with the unexpectedness of the result (see for example MPEP § 716.02(d)[R-1]). In order for such an argument to be valid, the argument must be commensurate in scope with the claimed invention. This is clearly not the instant case since the invention concerns the testing of more than just HERG1 and Kv1.5 in a *tok1Δ trk1Δ trk2Δ* triple mutant. Indeed, as set forth above, the fact that neither HERG1 nor Kv1.5 complements the double deletion strain (as alleged by Applicant) does not correlate to the non-complementation of any other eukaryotic potassium ion channel in the double deletion strain. Such a presumption is in fact disproved by the fact that at least one potassium ion channel, gpIRK1, *did* in fact complement the double deletion strain (as

taught by Tang). Thus, it is clear that the unexpected results that Applicant relies upon as an argument are not commensurate in scope with the instantly rejected claims.

In conclusion, Applicant's arguments are not convincing for several reasons. First, Applicant's allegation of teaching away (because the triple mutant is more compromised than the double mutant) is in fact the exact motivation that the ordinary skilled artisan would find in order to make the *tok1Δ trk1Δ trk2Δ* triple mutant. As set forth above, the ordinary skilled artisan would want the test cell to be in its most compromised state in order to most accurately perform the assay described by Gaber. Second, Applicant's claim that HERG1 and Kv1.5 would not be expected to rescue the triple mutant because, as taught by the instant specification, it cannot rescue the double mutant, was unknown to the skilled artisan at the time the combined references were publicly available. Additionally, the information that was available to the ordinary skilled artisan provided a strong motivation to combine the references, as set forth above and in the previous Office Actions. Furthermore, this arguments contradicts Applicant's own findings that HERG1 and Kv1.5 does indeed rescue the triple mutant; if Applicant is going to rely on their own teachings to try to traverse the motivation to combine references, they must rely on the complete teachings of their specification. Finally, even if Applicant's arguments were acceptable, they amount to an "unexpected results" argument that is not commensurate in scope with the claimed invention. In other words, the claimed invention is not drawn to a method of identifying inhibitors or activators of HERG1 or Kv1.5, which is where the unexpected result supposedly resides. In view of these facts, the rejection must be maintained over the instant claims.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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JAMES KETTER
PRIMARY EXAMINER